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2019-07

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Kivimäki , M , Nyberg , S T , Pentti , J , Madsen , I E H , Hanson , L L M , Rugulies , R ,  
Vahtera , J & Coggon , D 2019 , ' Individual and Combined Effects of Job Strain  
Components on Subsequent Morbidity and Mortality ' , Epidemiology , vol. 30 , no. 4 , pp.  
E27-E29 . <https://doi.org/10.1097/EDE.0000000000001020>

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<http://hdl.handle.net/10138/312905>

<https://doi.org/10.1097/EDE.0000000000001020>

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**Individual and Combined Effects of Job Strain Components on Subsequent Morbidity and Mortality**

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Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article ([www.epidem.com](http://www.epidem.com))

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To the Editor:

In analyses of longitudinal data from 7 to 14 cohort studies, the Individual Participant Data Meta-analysis in Working Populations (IPD-Work) consortium has demonstrated associations of job strain with increased risk of coronary heart disease (CHD),<sup>1</sup> ischaemic stroke,<sup>2</sup> type 2 diabetes,<sup>3</sup> and depression.<sup>4</sup> Moreover, among men who already had cardio-metabolic disease, job strain carried a 1.6-fold increased risk of death.<sup>5</sup> In contrast, no association was evident with other health outcomes, such as cancer, chronic obstructive pulmonary disease, asthma, Crohn's disease or ulcerative colitis (eAppendix, p. 2, <http://links.lww.com/EDE/B507>).

In all those analyses, job strain was defined by the combination of high occupational demands with low control,<sup>6</sup> and was selected for investigation because, based on psychological theory,<sup>7,8</sup> it was expected *a priori* to trigger harmful stress responses that might cause or promote chronic disease. Some commentators, however, have challenged this predefined approach and questioned the extent to which the observed associations with cardio-metabolic outcomes and depression reflect effects specific to job strain, or whether they might be driven by independent effects of high occupational demands or low job control.<sup>9</sup>

Here we address that concern by presenting further analyses of the IPD-Work datasets. We report separate risk estimates for each combination of occupational demands and control, taking the combination of 'neither high demands nor low control' as the reference. A description of the study populations and assessment of outcomes (i.e. CHD,<sup>1</sup> ischemic stroke,<sup>2</sup> type 2 diabetes,<sup>3</sup> depression<sup>4</sup> and, among men with cardio-metabolic disease, total mortality)<sup>5</sup> has been published previously, and is summarised in the eAppendix (p. 1-5, <http://links.lww.com/EDE/B507>).

The Table shows the results of previous IPD-Work studies on job strain as a binary exposure (part A) and those of the present analysis on job strain components (parts B and C). For each outcome, the summary risk estimates for job strain in the current component-specific analysis (part B) were similar in direction and magnitude to those previously published for the binary job strain variable (part A). In addition, age-, sex-, and socioeconomic status-adjusted hazard ratios for high demands with low control (i.e. job strain) were substantially higher than those for high demands in the absence of low control and low control in the absence of high demands (part B).

Study-specific analyses for incident CHD, ischemic stroke, type 2 diabetes, and clinical depression showed that 38 (83%) of the 46 hazard ratios for job strain vs. neither high demands nor low control favoured risk factor status (part C). According to  $I^2$ -statistics, heterogeneity in the study-specific hazard ratios was 0% for all outcomes (eAppendix, p. 5-10, <http://links.lww.com/EDE/B507>). Consistency of study-specific findings was poorer for high demands in the absence of low control (24/46 (52%), max  $I^2$ =19%) and low control in the absence of high demands (30/46 (65%), max  $I^2$ =53%). Small sample size precluded study-level comparisons for mortality in men with cardio-metabolic disease.

In conclusion, findings of cohort studies from the UK, France, Belgium, Denmark, Sweden, and Finland indicate that for each of CHD, ischemic stroke, type 2 diabetes, depression and (among men with cardio-metabolic disease) mortality, risks are highest in individuals with job strain, whereas any effects of high occupational demands in the absence of low control, and of low job control in the absence of high demands, were weaker. Job strain defined as the combination of high job demands and low control is consistent with more general definitions of psychological stress which suggest that stress occurs when demands from external situations are perceived to be beyond coping capacities.<sup>7</sup> As such, our

results support the psychological stress theory underpinning our *a priori* decision to examine job strain as a binary risk factor for morbidity and mortality.

[597 words]

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**Table. Adjusted Hazard Ratios for the Association of Binary Job Strain Variable with Morbidity and Mortality in Previous IPD-Work Studies (A) and Age-, Sex-, and Socioeconomic Status-adjusted Hazard Ratios for the Associations of Job Strain Components with These Outcomes (B, C).**

	Hazard ratio (95% confidence interval)				
	Coronary heart disease	Ischemic stroke	Type 2 diabetes	Depression	Death (in men with pre-existing cardiometabolic disease)
<b>A. Published estimates for job strain as a binary exposure<sup>1-5a</sup></b>					
No job strain (reference)	1.00	1.00	1.00	1.00	1.00
Job strain	1.17 (1.05 – 1.31)	1.18 (1.00 – 1.39)	1.15 (1.06 – 1.25)	1.22 (1.02 – 1.47)	1.66 (1.23 – 2.25)
Published IPD-Work paper	1	2	3	4	5
<b>B. Summary estimates for combined effects of job strain components</b>					
Neither high demands nor low control (reference)	1.00	1.00	1.00	1.00	1.00
High demands in the absence of low control	1.09 (0.97 – 1.23)	1.03 (0.86 – 1.24)	0.98 (0.90 – 1.08)	1.04 (0.86 – 1.25)	0.98 (0.72 – 1.34)
Low control in the absence of high demands	1.07 (0.90 – 1.27)	1.09 (0.89 – 1.33)	0.97 (0.81 – 1.15)	1.18 (0.99 – 1.41)	1.20 (0.88 – 1.64)
High demands and low control (i.e. job strain)	1.21 (1.05 – 1.39)	1.16 (0.94 – 1.42)	1.13 (1.02 – 1.25)	1.29 (1.06 – 1.56)	1.69 (1.19 – 2.42)
N (cases)	1965	909	3703	982	307
N (total)	126,078	111,681	124,808	120,221	1975
<b>C. Study-specific estimates<sup>b</sup></b>					
	Number of studies				
High demands in the absence of low control					
Studies favouring increased risk	7	5	7	5	-
Studies favouring reduced risk	3	4	6	9	-
Low control in the absence of high demands					
Studies favouring increased risk	7	6	7	10	-
Studies favouring reduced risk	3	3	6	4	-
High demands and low control (i.e. job strain)					
Studies favouring increased risk	9	6	12	11	-
Studies favouring reduced risk	1	3	1	3	-

<sup>a</sup>Published estimates are as shown in IPD-Work papers.<sup>1-5</sup> The estimates are adjusted for age, sex, and socioeconomic status with the exception of depression (additionally adjusted for cohabitation) and death in men (adjusted for age and study). 'No job strain' category includes combinations of 'neither high demands nor low control', 'low control in the absence of high demands' and 'high demands in the absence of low control'.

<sup>b</sup>Hazard ratios >1 favour increased risk and hazard ratios <1 favour reduced risk. Study-level hazard ratios were not available for mortality as the analyses were on pooled data due to small numbers.<sup>5</sup>